Ghosal hematodiaphyseal dysplasia

Ghosal hematodiaphyseal dysplasia is a rare inherited condition characterized by abnormally thick bones and a shortage of red blood cells (anemia). Signs and symptoms of the condition become apparent in early childhood.

In affected individuals, the long bones in the arms and legs are unusually dense and wide. The bone changes specifically affect the shafts of the long bones, called diaphyses, and areas near the ends of the bones called metaphyses. The bone abnormalities can lead to bowing of the legs and difficulty walking.

Ghosal hematodiaphyseal dysplasia also causes scarring (fibrosis) of the bone marrow, which is the spongy tissue inside long bones where blood cells are formed. The abnormal bone marrow cannot produce enough red blood cells, which leads to anemia.Signs and symptoms of anemia that have been reported in people with Ghosal hematodiaphyseal dysplasia include extremely pale skin (pallor) and excessive tiredness (fatigue).

Frequency

Ghosal hematodiaphyseal dysplasia is a rare disorder; only a few cases have been reported in the medical literature. Most affected individuals have been from the Middle East and India.

Genetic Changes

Ghosal hematodiaphyseal dysplasia results from mutations in the *TBXAS1* gene. This gene provides instructions for making an enzyme called thromboxane A synthase 1, which acts as part of a chemical signaling pathway involved in normal blood clotting (hemostasis). Based on its role in Ghosal hematodiaphyseal dysplasia, researchers suspect that thromboxane A synthase 1 may also be important for bone remodeling, which is a normal process in which old bone is removed and new bone is created to replace it, and for the production of red blood cells in bone marrow.

Mutations in the *TBXAS1* gene severely reduce the activity of thromboxane A synthase 1. Studies suggest that a lack of this enzyme's activity may lead to abnormal bone remodeling and fibrosis of the bone marrow. However, the mechanism by which a shortage of thromboxane A synthase 1 activity leads to the particular abnormalities characteristic of Ghosal hematodiaphyseal dysplasia is unclear.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- diaphyseal dysplasia associated with anemia
- GHDD
- Ghosal hemato-diaphyseal dysplasia
- Ghosal syndrome
- Ghosal-type hemato-diaphyseal dysplasia

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Ghosal syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1856465/

Other Diagnosis and Management Resources

- National Heart, Lung, and Blood Institute: How is Anemia Diagnosed?
  https://www.nhlbi.nih.gov/health/health-topics/topics/anemia/diagnosis
- National Heart, Lung, and Blood Institute: How is Anemia Treated?
  https://www.nhlbi.nih.gov/health/health-topics/topics/anemia/treatment

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Anemia
  https://medlineplus.gov/ency/article/000560.htm
- Health Topic: Anemia
  https://medlineplus.gov/anemia.html
- Health Topic: Bone Diseases
  https://medlineplus.gov/bonediseases.html

Genetic and Rare Diseases Information Center

- Ghosal hematodiaphyseal dysplasia syndrome
  https://rarediseases.info.nih.gov/diseases/10297/ghosal-hematodiaphyseal-dysplasia-syndrome

Additional NIH Resources

- National Heart, Lung, and Blood Institute: What is Anemia?
  https://www.nhlbi.nih.gov/health/health-topics/topics/anemia/

Educational Resources

- Cedars-Sinai Health System: Skeletal Dysplasia
  http://www.cedars-sinai.edu/Patients/Health-Conditions/Skeletal-Dysplasia.aspx
- Disease InfoSearch: Ghosal Syndrome
  http://www.diseaseinfosearch.org/Ghosal+Syndrome/3039
- KidsHealth from Nemours: Anemia
  http://kidshealth.org/en/parents/anemia.html
- Orphanet: Ghosal hematodiaphyseal dysplasia
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1802

Patient Support and Advocacy Resources

- Resource List from the University of Kansas Medical Center: Dwarfism/Short Stature and Skeletal Dysplasias
  http://www.kumc.edu/gec/support/skeldysp.html
- The MAGIC Foundation
  https://www.magicfoundation.org/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Ghosal%5BTI%5D%29

OMIM

- GHOSAL HEMATODIAPHYSEAL DYSPLASIA
  http://omim.org/entry/231095

Sources for This Summary

- Geneviève D, Proulle V, Isidor B, Bellais S, Serre V, Djouadi F, Picard C, Vignon-Savoye C, Bader-Meunier B, Blanche S, de Vernejoul MC, Legeai-Mallet L, Fischer AM, Le Merrer M, Dreyfus M, Gaussem P, Munnich A, Cormier-Daire V. Thromboxane synthase mutations in an increased bone density disorder (Ghosal syndrome). Nat Genet. 2008 Mar;40(3):284-6. doi: 10.1038/ng.2007.66. Epub 2008 Feb 10.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18264100
- Ghosal SP, Mukherjee AK, Mukherjee D, Ghosh AK. Diaphyseal dysplasia associated with anemia. J Pediatr. 1988 Jul;113(1 Pt 1):49-57. Erratum in: J Pediatr 1988 Aug;113(2):410.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/3385529
- Gümrük F, Besim A, Altay C. Ghosal haemato-diaphyseal dysplasia: a new disorder. Eur J Pediatr. 1993 Mar;152(3):218-21.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/8444247
- Isidor B, Dagoneau N, Huber C, Genevieve D, Bader-Meunier B, Blanche S, Picard C, De Vernejoul MC, Munnich A, Le Merrer M, Cormier-Daire V. A gene responsible for Ghosal hemato-diaphyseal dysplasia maps to chromosome 7q33-34. Hum Genet. 2007 Apr;121(2):269-73. Epub 2007 Jan 3.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17203301

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